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09/785,514	02/16/2001	Jian-Bing Fan	A-68970-1/DJB/RMS/DCF	5362

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EXAMINER	
FORMAN, BETTY J	
ART UNIT	**PAPER NUMBER**
1634	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/785,514	FAN ET AL.	
	Examiner	Art Unit	
	BJ Forman	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34* is/are pending in the application.

4a) Of the above claim(s) *1-13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8/02, 5/01*.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *0304* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Notice of Withdrawal*.

DETAILED ACTION

1. Prosecution on the merits of this application is reopened on claims 14-34 are considered unpatentable for the reasons indicated below.

Amendments

2. The amendments to the specification submitted 23 December 2003 under Rule 312 are acknowledged. The amendments have been thoroughly reviewed and entered.

The Terminal Disclaimer filed 25 November 2003 has been approved.

Status of the Claims

3. Claims 1-34 are pending.

Claims 1-14 are withdrawn from prosecution.

Claims 14-34 are under prosecution.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 21, 22, 27-28, 33-34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 21, 22, 27-28, 33-34 are indefinite in Claim 21 because the claim is drawn to a method of genotyping. However, the claims do not recited method steps of genotyping or gene analysis. As such, it is unclear whether the method steps achieve the claimed method.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

7. Claims 14, 16, 27, 28 and 30 rejected under 35 U.S.C. 102(e) as being anticipated by Walt et al (U.S. Patent No. 6,327,410, filed 11 September 1998).

Regarding Claim 14, Walt et al disclose the method comprising providing an array composition comprising a substrate having discrete sites and a population of microspheres containing first and second subpopulations wherein each microsphere comprises a plurality of

different target analytes e.g. antibodies and antigens (see Fig. 3) wherein the microspheres are distributed on the surface. The method further comprising contacting the array with a first set of read out probes e.g. labeled antibodies (Column 23, lines 2-7) to detect the presence of a first target analyte (Column 4, lines 35-58 and Column 15, lines 30-63). Walt et al specifically teach their method wherein each microsphere comprises a proteinaceous target analyte and an analyte for the proteinaceous target i.e. labeled antibody (Column 23, lines 2-7). Hence, they teach the microspheres wherein each microsphere comprises a plurality (i.e. 2) different analytes as claimed.

Regarding Claim 16, Walt et al disclose the method wherein the microspheres are randomly distributed on the surface (Column 4, lines 53-56).

Regarding Claim 27, Walt et al disclose the method wherein the substrate is a fiber optic bundle (Column 5, lines 57-60).

Regarding Claim 28, Walt et al disclose the method wherein the substrate is selected from glass and plastic (Column 5, lines 57-60).

Regarding Claim 30, Walt et al disclose the method wherein the target analyte comprise target sequences i.e. the proteinaceous and antibody targets are comprised of amino acid sequences and therefor comprise target sequences.

8. Claims 14-34 are rejected under 35 U.S.C. 102(e) as being anticipated by Chee et al (U.S. Patent No. 6,355,431, filed 3 March 2000 and claiming priority to 20 May 1999).

The applied reference has a common inventor and assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under

35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Regarding Claim 14, Chee et al disclose the method comprising providing an array composition comprising a substrate having discrete sites and a population of microspheres containing first and second subpopulations wherein each microsphere comprises a plurality of different target analytes (i.e. capture probe and modified primer) wherein the microspheres are distributed on the surface. The method further comprising contacting the array with a first set of read out probes (e.g. amplifier probes, Column 34, line 32-Column 36, line 14) to detect the presence of a first target analyte (Claim 1).

Regarding Claim 15, Chee et al disclose the method further comprising contacting the array composition with a second set of readout probes (Column 35, lines 23-57 and Column 36, lines 15-23).

Regarding Claim 16, Chee et al disclose the method wherein the microspheres are randomly distributed on the surface (Claim 30).

Regarding Claim 17, Chee et al disclose the method wherein the first set of readout probes comprises at least first and second probes wherein the first and second probes are differentially labeled (Column 35, lines 42-57).

Regarding Claim 18, Chee et al disclose the method further comprising detecting the firs label as an indication of the first target analyte (Column 35, lines 42-57).

Regarding Claim 19, Chee et al disclose the method wherein the first and second subpopulations comprise analytes from first and second sources e.g. multiplex detection of different polymorphisms (Column 56, line 63-Column 57, line 19).

Regarding Claim 20, Chee et al disclose the method wherein the different sources are patients (Column 56, lines 23-32).

Regarding Claim 21, Chee et al disclose the method of genotyping comprising providing an array composition comprising a substrate having discrete sites and a population of microspheres containing first and second subpopulations wherein each microsphere comprises a plurality of different target analytes (i.e. capture probe and modified primer) wherein the microspheres are randomly distributed on the surface. The method further comprising contacting the array with a first set of extension probes that hybridize adjacent to a detection position, contacting with a nucleotide and an polymerase to extend the extension probe and detecting the presence of the nucleotide (Fig. 2A/2B and Claim 5).

Regarding Claim 22, Chee et al disclose the method wherein the nucleotide comprises a label (Fig. 2A/2B and Column 6, lines 9-16).

Regarding Claim 23, Chee et al disclose the method of determining the identification of a nucleotide comprising providing an array composition comprising a substrate having discrete sites and a population of microspheres containing first and second subpopulations wherein each microsphere comprises a plurality of different target analytes (i.e. capture probe and modified primer) wherein the microspheres are randomly distributed on the surface. The method further comprising forming hybridization complex between the target sequence and a readout probe and determining the nucleotide at the detection position label (Fig. 2A/2B; Column 6, lines 9-16; and Claim 5).

Regarding Claim 24, Chee et al disclose the method wherein the target comprises a first and second target domain and the hybridization complex comprises a first readout probe hybridized to the first domain and a second readout probe hybridized to the second domain and said determining comprising adding a ligase (Column 17, line 55-Column 18, line 67 and Claim 6).

Regarding Claim 25, Chee et al disclose the method wherein the first readout probe comprises a label (Column 17, line 55-Column 18, line 67).

Regarding Claim 26, Chee et al disclose the method further comprising contacting the hybridization complex with at least a first nucleotide and a polymerase to extend the first readout probe wherein the nucleotide is complementary to the detection position (Column 18, lines 9-18).

Regarding Claim 27, Chee et al disclose the method wherein the substrate is a fiber optic bundle (Claim 28).

Regarding Claim 28, Chee et al disclose the method wherein the substrate is glass or plastic (Claim 29).

Regarding Claim 29, Chee et al disclose the method further comprising contacting the microspheres with decoder binding ligands and the microspheres comprise identifier binding ligand (Column 49, lines 16-20).

Regarding Claim 30, Chee et al disclose the method wherein the target comprises target sequences (Column 9, lines 14-25).

Regarding Claim 31, Chee et al disclose the method wherein the target sequences comprises target nucleic acids (Column 9, lines 14-25).

Regarding Claim 32, Chee et al disclose the method wherein the target comprises target genomic DNA sequences (Column 9, lines 14-25).

Regarding Claim 33, Chee et al disclose the method wherein the target sequences comprises target nucleic acids (Column 9, lines 14-25).

Regarding Claim 34, Chee et al disclose the method wherein the target nucleic acids comprises target genomic DNA (Column 9, lines 14-25).

9. Claims 14-18, 21-26, 28, 30-34 are rejected under 35 U.S.C. 102(b) as being anticipated by Brenner et al (U.S. Patent No. 5,846,719, issued 8 December 1998).

Regarding Claim 14, Brenner et al disclose the method comprising providing an array composition comprising a substrate having discrete sites (Column 16, lines 26-30) and a population of microspheres containing first and second subpopulations wherein each microsphere comprises a plurality of different target analytes (i.e. oligo tag and e.g. cDNA) wherein the microspheres are distributed on the surface (Column 26, line 52-Column 27, line 30). The method further comprising contacting the array with a first set of read out probes to detect the presence of a first target analyte (Column 4, lines 16-60; Column 23, line 65-Column 25, line 21; and Example 2, Columns 35-38).

Regarding Claim 15, Brenner et al disclose the method further comprising contacting the array composition with a second set of readout probes (Column 23, lines 35-57).

Regarding Claim 16, Brenner et al disclose the method wherein the microspheres are randomly distributed on the surface (Column 26, lines 48-52).

Regarding Claim 17, Brenner et al disclose the method wherein the first set of readout probes comprises at least first and second probes wherein the first and second probes are differentially labeled (Column 37, lines 8-32).

Regarding Claim 18, Brenner et al disclose the method further comprising detecting the first label as an indication of the first target analyte (Column 37, line 8-Column 38, line 2).

Regarding Claim 21, Brenner et al disclose the method of genotyping comprising providing an array composition comprising a substrate having discrete sites and a population of microspheres containing first and second subpopulations wherein each microsphere comprises a plurality of different target analytes (i.e. oligo tag and polynucleotide) wherein the microspheres are randomly distributed on the surface (Column 26, lines 48-52). The method further comprising contacting the array with a first set of extension probes that hybridize adjacent to a detection position, contacting with a nucleotide and an polymerase to extend the

extension probe and detecting the presence of the nucleotide (Column 30, line 66-Column 31, line 25).

Regarding Claim 22, Brenner et al disclose the method wherein the nucleotide comprises a label (Column 30, line 66-Column 31, line 25).

Regarding Claim 23, Brenner et al disclose the method of determining the identification of a nucleotide comprising providing an array composition comprising a substrate having discrete sites and a population of microspheres containing first and second subpopulations wherein each microsphere comprises a plurality of different target analytes (i.e. oligo tag and polynucleotide) wherein the microspheres are distributed on the surface (Column 26, line 52-Column 27, line 30).. The method further comprising forming hybridization complex between the target sequence and a readout probe and determining the nucleotide at the detection position label (Column 4, lines 16-60; Column 23, line 65-Column 25, line 21; and Example 2, Columns 35-38).

Regarding Claim 24, Brenner et al disclose the method wherein the target comprises a first and second target domain and the hybridization complex comprises a first readout probe hybridized to the first domain and a second readout probe hybridized to the second domain and said determining comprising adding a ligase (Column 34, lines 1-28 and Example 2, Column 37).

Regarding Claim 25, Brenner et al disclose the method wherein the first readout probe comprises a label (Column 37, lines 8-31).

Regarding Claim 26, Brenner et al disclose the method further comprising contacting the hybridization complex with at least a first nucleotide and a polymerase to extend the first readout probe wherein the nucleotide is complementary to the detection position (Column 30, line 66-Column 31, line 25).

Regarding Claim 28, Brenner et al disclose the method wherein the substrate is glass (Column 36, lines 43-45).

Regarding Claim 30, Brenner et al disclose the method wherein the target comprises target sequences (Column 5, lines 13-21 and Column 33, lines 5-11).

Regarding Claim 31, Brenner et al disclose the method wherein the target sequences comprises target nucleic acids (Column 5, lines 13-21 and Column 33, lines 5-11).

Regarding Claim 32, Brenner et al disclose the method wherein the target comprises target genomic DNA sequences (Column 33, lines 5-11).

Regarding Claim 33, Brenner et al disclose the method wherein the target sequences comprises target nucleic acids (Column 5, lines 13-21 and Column 33, lines 5-11).

Regarding Claim 34, Brenner et al disclose the method wherein the target nucleic acids comprises target genomic DNA (Column 33, lines 5-11).

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. Claims 19, 20, 27 and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brenner et al (U.S. Patent No. 5,846,719, issued 8 December 1998) and Walt et al (U.S. Patent No. 6,327,410, filed 11 September 1998).

Regarding Claims 19 and 20, Brenner et al disclose the method comprising providing an array composition comprising a substrate having discrete sites (Column 16, lines 26-30) and a population of microspheres containing first and second subpopulations wherein each microsphere comprises a plurality of different target analytes (i.e. oligo tag and e.g. cDNA) wherein the microspheres are distributed on the surface (Column 26, line 52-Column 27, line 30). The method further comprising contacting the array with a first set of read out probes to detect the presence of a first target analyte (Column 4, lines 16-60; Column 23, line 65-Column 25, line 21; and Example 2, Columns 35-38).

Walt et al disclose a similar method comprising providing an array composition comprising a substrate having discrete sites and a population of microspheres containing first and second subpopulations wherein each microsphere comprises a plurality of target analytes, wherein the microspheres are distributed on the surface and further comprising contacting the array with a first set of read out probes to detect the presence of a first target analyte (Column 3, lines 35-54 and Column 24, lines 3-52) wherein the array screens "patient**s**" for multiple diseases and conditions (Column 24, lines 14-22) which clearly suggests that first and second target analytes are from first and second patients as claimed.

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to use the methods of Brenner et al and Walt et al to analyze targets from multiple patients as suggested by Walt et al for the obvious benefits of multiplex screening as desired by Walt et al (Column 24, lines 14-22 and Column 25, lines 2-10).

Regarding Claim 27, Brenner et al disclose the method wherein the substrate is selected for optimal detection as known in the art (Column 25, lines 42-54) but they do not teach a fiber optic bundle substrate. However, Walt et al teach the similar method wherein the preferred substrate is a fiber optic bundle (Column 6, lines 32-40) wherein the fiber optic bundle substrate permits randomly mixed and distributed microspheres carrying different functionalities to be mixed while the ability to individually detect and identify microsphere

functionality is maintained (Column 4, lines 35-40). Walt further teaches that this property of the fiber optic bundle provides for fast and inexpensive array construction. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the fiber optic bundle substrate of Walt et al to the substrate of Brenner et al. One of ordinary skill in the art would have been motivated to utilize the fiber optic bundle of Walt et al to thereby save time and money based on the fast and inexpensive array construction taught by Walt et al (Column 4, lines 53-58).

Regarding Claim 29, Brenner et al do not teach decoder binding ligands. However, Walt et al teach the similar method wherein decoder binding ligands e.g. intercalators bind identifier binding ligand on the microsphere i.e. double stranded nucleic acids for identification of the target analyte wherein intercalators are preferred addition because they identify the presence of target hybridization (Column 21, lines 52-60). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the intercalators of Walt et al to the target identification of Brenner et al based on the preferred teaching of Walt et al and for the expected benefit of detecting the presence of target hybridization (Walt et al, Column 21, lines 52-60).

Conclusion

12. The examiner for this application has changed. Please address future correspondence to Examiner Forman, Art Unit: 1634.

13. No claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (703) 306-5878. The examiner can normally be reached on 6:00 TO 3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (703) 308-1119. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

BJ Forman, Ph.D.
Primary Examiner
Art Unit: 1634
March 10, 2004